

CLAIMS

What Is Claimed Is:

1. A combinatorial library of indolinone
compounds, comprising a series of at least ten indolinones
5 that can be formed by reacting oxindoles with aldehydes.

2. The combinatorial library of claim 1 wherein
said oxindoles are type A oxindoles.

3. The combinatorial library of claim 1 wherein
said aldehydes are type B aldehydes.

10 4. The combinatorial library of claim 1 wherein
said library comprises at least 100 indolinones.

5. The combinatorial library of claim 1 wherein
said library comprises at least 1000 indolinones.

15 6. The combinatorial library of claim 1,
wherein most of said indolinones are in the cis
conformation.

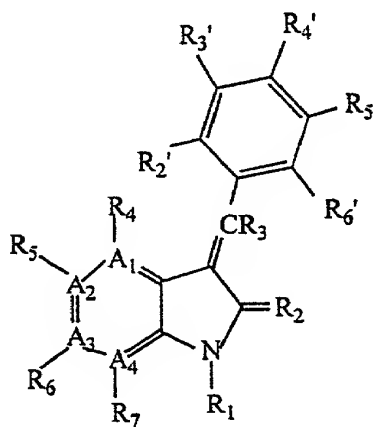
7. A method of making an indolinone comprising
the steps of

(a) creating a combinatorial library of

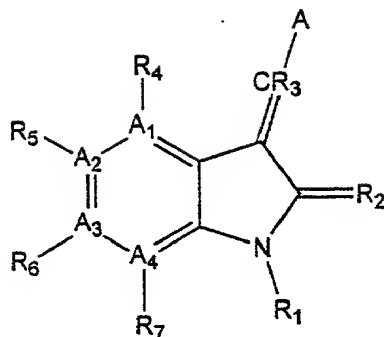
indolinones by reacting a series of
oxindoles with a series of aldehydes,

- (b) testing said indolinones in biological assays,
(c) selecting one or more indolinones with favorable
activity; and
(d) synthesizing one or more of said indolinones
selected in step (c).

8. A compound having formula V or VI



(V)



(VI)

and pharmaceutically acceptable salts, isomers,
 5 metabolites, esters, amides, and prodrugs thereof, wherein:

(a) A₁, A₂, A₃, and A₄ are independently carbon or
 nitrogen;

(b) R₁ is hydrogen or alkyl;

(c) R₂ is oxygen or sulfur;

(d) R₃ is hydrogen;

10 (e) R₄, R₅, R₆, and R₇ are optionally present and are
 each independently selected from (i) the group consisting
 of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl,
 alkaryloxy, halogen, trihalomethyl, S(O)R, SO₂NRR', SO₃R,
 15 SR, NO₂, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH₂)_nCO₂R,
 and CONRR' or (ii) any two adjacent R₄, R₅, R₆, and R₇ taken
 together form a fused ring with the aryl portion of the
 oxindole-based portion of the indolinone;

(f) R₂', R₃', R₄', R₅', and R₆' are each independently

selected from the group consisting of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO₂NRR', SO₃R, SR, NO₂, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH₂)_nCO₂R, and CONRR';

5 (g) n is 0, 1, 2, or 3;

(h) R is H, alkyl or aryl; and

(i) R' is H, alkyl or aryl.

10 (j) A is a five membered heteroaryl ring selected from the group consisting of thiophene, pyrrole, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, oxazole, isoxazole, thiazole, isothiazole, furan, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3,4-oxatriazole, 1,2,3,5-oxatriazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3,4-thiatriazole, 1,2,3,5-thiatriazole, and tetrazole, optionally substituted at one or more positions with alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO₂NRR', SO₃R, SR, NO₂, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH₂)_nCO₂R or
15
20 CONRR'.

9. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and a compound according to Claim 8.

25 10. A method for treating diseases related to unregulated tyrosine kinase signal transduction, the method

comprising the step of administering to a subject in need thereof a therapeutically effective amount of a compound according to Claim 8.

- 5 11. A method for regulating tyrosine kinase signal transduction comprising administering to a subject a therapeutically effective amount of a compound according to Claim 8.